

<p align="center">Advisory Action Before the Filing of an Appeal Brief</p>	<p>Application No. 10/595,821</p>	<p>Applicant(s) VERBRUGGEN ET AL.</p>	
	<p>Examiner Kade Ariani</p>	<p>Art Unit 1651</p>	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 May 2010 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: 23-27,30,31,37-40 and 43-49.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Continuation of 11. does NOT place the application in condition for allowance because: Claims remain rejected for the reasons of record, (see Attached).

Attachment to the Advisory Action:

Applicant argues that because Verbruggen teaches xylosan polysulfate and chondroitin polysulfate but not heparin, significantly increase aggrecan aggregate sizes, therefore Verbruggen teaches away from using heparin-like molecules interchangeably in chondrocyte cultivation. Applicant argues that Verbruggen concludes that heparin-like molecules have different or unpredictable effects on chondrocyte development (see Remarks page 3 2nd -4th paragraphs filed on 05/04/2010). These arguments are considered but are not found persuasive because Verbruggen et al. do not teach xylosan polysulfate and chondroitin polysulfate are heparin-like molecules (or heparinoids), instead Verbruggen et al. teach xylosan polysulfate, chondroitin polysulfate are polysulphated polysaccharides. Verbruggen et al. teach polysulphated polysaccharides, xylosan polysulfate, chondroitin polysulfate, increased the synthesis of high molecular weight hyaluronan by chondrocyte. Verbruggen et al. further teach stimulation of the production of high molecular weight hyaluronan by chondrocytes seems to be a common effect of polysulfated polysaccharides (p1669 1st column 5th paragraph lines 24-28).

Moreover, Verbruggen et al. teach polysulphated polysaccharides, xylosan polysulfate and chondroitin polysulfate, consistently improved aggrecan synthesis in the culture chondrocytes, and heparin was less active on these cells (page 1669 1st column 4th paragraph lines 1-4). Therefore, Verbruggen et al. neither teach away from using heparin (or heparin-like molecules) in chondrocyte cultivation nor concludes that heparin-like molecules have unpredictable effects on chondrocyte development, as alleged by the Applicant.

Applicant argues that one of ordinary skill in the art would have not been motivated to combine Verbruggen and Rosenberg teachings and that the combination of references fails to provide a motivation to use polysulphated alginate for chondrocyte cultivation (see Remarks page 3 4th paragraphs filed on 05/04/2010). These arguments are considered but are not found persuasive because Rosenberg et al. teach polysulfates prepared from alginic acid (polysulphated alginate) and chondroitin polysulphates are polysulfated polysaccharides, which are non-thrombogenic (heparin-like effect). Rihova teach a matrix suitable for implantation, must be non-thrombogenic (anticoagulant activity) to be biocompatible. Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to try (choosing from a finite number of identified polysulfated polysaccharides) and to use polysulfated polysaccharide, polysulphated alginate, in the method and the composition as taught by Verbruggen et al. with a reasonable expectation of success in providing an in vitro method for cultivation of chondrogenic cells, a composition comprising polysulphated alginate, and a method of treatment of cartilage defects. The motivation as taught by Verbruggen et al. would be stimulation of the production of high molecular weight hyaluronan by chondrocytes seems to be a common effect of polysulfated polysaccharides.